

5. Applicants note with appreciation that any rejection that is not expressly maintained in this Office Action has been withdrawn.

6-7. The claims are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to enable one of skill in the art to practice the claimed invention. The claims are further rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. Applicants traverse these rejections to the extent that they are maintained in light of the amended claims.

Applicants maintain the arguments of record and contend that the application as filed, as well as the extensive post-filing evidence, provide adequate written description and an enabling disclosure to support claims directed to the treatment of a variety of peripheral neuropathies using both hedgehog polypeptides and variant hedgehog polypeptides. Nevertheless, to expedite prosecution of claims directed to commercially relevant embodiments of Applicants' invention, Applicants have amended the claims. Applicants' amendments to the claims are consistent with the recommendations provided by the Examiner in the last Office Action (see, page 3). However, Applicants' amendments do not indicate acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

8-9. The claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that Applicants' regard as the invention. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

The previous basis of the rejection appears to have been an alleged ambiguity in the recitation of the term "the N-terminal amino acid residue." However, Applicants contend that this term is routinely used in the art to refer to the most N-terminally situated amino acid residue in a polypeptide chain, and that one of skill would instantly recognize what is meant by the term. Furthermore, Applicants contend that as the claims are now directed to polypeptides comprising amino acid sequences explicitly recited in the application, there can be no doubt as to which residue in a particular polypeptide chain is referred to as the N-terminal amino acid residue.

Accordingly, Applicants contend that one of skill in the art can readily appreciate the metes and bounds of the claimed subject matter. Recitation of the term "the N-terminal amino acid residue" would be readily appreciated in any context, and when provided the additional guidance offered by the specification and the claims, there can certainly be no doubt as to what is claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

10-11. The claims are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. The claims are similarly objected to under 35 U.S.C. 132 for allegedly introducing new matter. Applicants traverse this rejection and this objection to the extent that they are maintained in light of the amended claims.

The basis of both the rejection and objection is the explicit recitation of "two or more lipophilic moieties", and the Examiner's allegation that the specification lacks support for this term. The Examiner appears to be basing this concern on the alleged lack of *in haec verba* support in the specification for this phrase. However, in accordance with MPEP 2163, the specification need not provide *in his verbis* support for the claimed subject matter. All that is required is that "newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." (MPEP 2163). Applicants contend that the specification provides ample implied and inherent support for claims directed to two or more lipophilic moieties, and accordingly Applicants contend that the pending claims satisfy all of the requirements under 35 U.S.C. 112, first paragraph.

Nevertheless, to expedite prosecution of claims directed to commercially relevant embodiments of the invention, Applicants have amended the claims to recite "one or more lipophilic moieties." Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Furthermore, Applicants point out that recitation of "one or more lipophilic moieties" is actually broader in scope than recitation of "two or more lipophilic moieties", and accordingly Applicants' amendments should not be construed to narrow the scope of the remaining claims. In light of

Applicants' amendments, reconsideration and withdrawal of the rejection and the objection are respectfully requested.

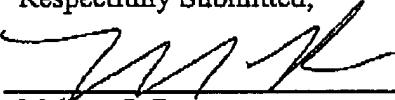
**CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to Deposit Account No. 18-1945.

Respectfully Submitted,

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